For the treatment of moderate-to-severe dyspareunia and vaginal dryness, symptoms of vulvar and vaginal atrophy, due to menopause

Her dry spell could be coming to an end.

INTRODUCING | NEW

Bithena™

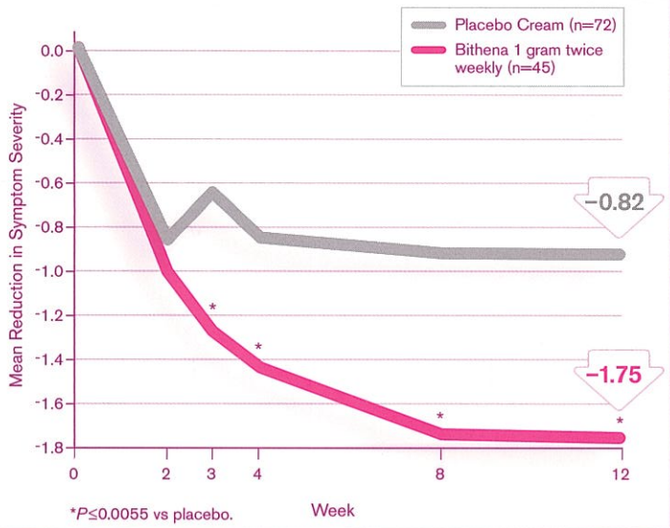
(synthetic conjugated estrogens, A) vaginal cream

Bring comfort back.

When moderate-to-severe symptoms of vulvar and vaginal atrophy due to menopause interrupt her life...

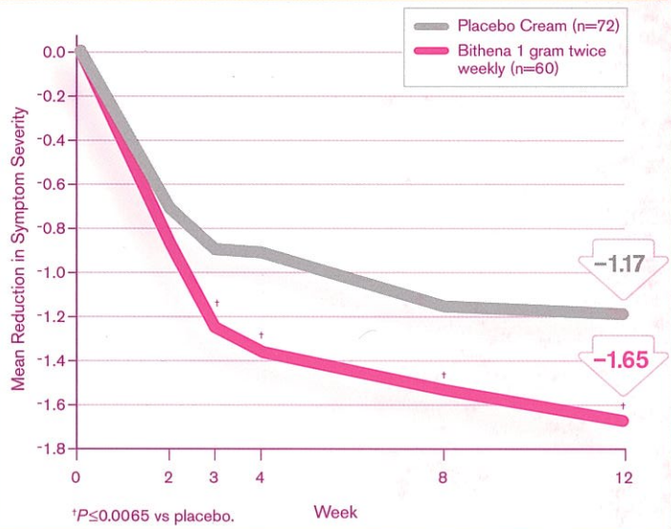
Bithena™ reduces dyspareunia and vaginal dryness to bring comfort back[1]

Mean Reduction in Dyspareunia[1]



*$P \leq 0.0055$ vs placebo.

Mean Reduction in Vaginal Dryness[1]



†$P \leq 0.0065$ vs placebo.

Mean reduction in symptom severity of patient-assessed most bothersome symptom (MBS) calculated from a severity scale: 3=severe; 2=moderate; 1=mild; 0=none. MBS was defined as the single moderate-to-severe symptom identified by the patient as most bothersome to her at baseline.[1]

Bithena Vaginal Cream is indicated for the treatment of moderate-to-severe dyspareunia and vaginal dryness, symptoms of vulvar and vaginal atrophy, due to menopause.[1]

Important Safety Information

ENDOMETRIAL CANCER

There is an increased risk of endometrial cancer in a woman with a uterus who uses unopposed estrogens. Adding a progestin to estrogen therapy has been shown to reduce the risk of endometrial hyperplasia, which may be a precursor to endometrial cancer. Adequate diagnostic measures, including endometrial sampling when indicated, should be undertaken to rule out malignancy in postmenopausal women with undiagnosed persistent or recurring abnormal vaginal bleeding.

CARDIOVASCULAR DISORDERS, BREAST CANCER, AND PROBABLE DEMENTIA

Estrogens with or without progestins should not be used for the prevention of cardiovascular disease or dementia.

The estrogen-alone substudy of the Women's Health Initiative (WHI) reported increased risks of stroke and deep vein thrombosis (DVT) in postmenopausal women (50 to 79 years of age) during 7.1 years of treatment with daily oral conjugated estrogens (CE 0.625 mg) relative to placebo.

The WHI estrogen plus progestin substudy reported increased risks of DVT, pulmonary embolism, stroke, myocardial infarction, and invasive breast cancer in postmenopausal women (50 to 79 years of age) during 5.6 years of treatment with daily oral conjugated estrogens (CE 0.625 mg) combined with medroxyprogesterone acetate (MPA 2.5 mg) per day, relative to placebo.

The Women's Health Initiative Memory Study (WHIMS), an ancillary study of the WHI study, reported increased risk of developing probable dementia in postmenopausal women 65 years of age or older during 5.2 years of treatment with CE 0.625 mg alone and during 4 years of treatment with

Get comfortable with Bithena™

- Supports vaginal health by increasing thickness of the vaginal epithelium and normalizing vaginal pH[1]
- Low systemic absorption of estradiol
  - 7.9 pg/mL at day 27[1]
- Formulated from plant-derived estrogens
  - Contains 0.625 mg synthetic conjugated estrogens, A per gram‡[1]
- Cream formulation can be directly applied to vaginal and vulvar tissues for soothing relief

In a 12-week, prospective, randomized, double-blind, placebo-controlled, multicenter study (N=275), the efficacy and safety of Bithena Vaginal Cream for the treatment of moderate-to-severe symptoms of vulvar and vaginal atrophy were compared with placebo. All patients were assessed for improvement in the mean change from baseline to Week 12 for the co-primary efficacy variables of most bothersome symptom of vulvar and vaginal atrophy; percentage of vaginal superficial cells and percentage of vaginal parabasal cells on a vaginal smear; and vaginal pH.[1]

Please see enclosed tolerability data.

Tolerability

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‡Use of estrogen, alone or in combination with a progestin, should be at the lowest effective dose and for the shortest duration consistent with treatment goals and risks for the individual woman. Postmenopausal women should be re-evaluated periodically as clinically appropriate (eg, at 3-month to 6-month intervals) to determine if treatment is still necessary.[1]

CE 0.625 mg combined with MPA 2.5 mg, relative to placebo. It is unknown whether this finding applies to younger postmenopausal women.

In the absence of comparable data, these risks should be assumed to be similar for other doses of CE and MPA therapy and other combinations and dosage forms of estrogens and progestins. Because of these risks, estrogens with or without progestins should be prescribed at the lowest effective doses and for the shortest duration consistent with treatment goals and risks for the individual woman.

Bithena Vaginal Cream should not be used in women with any of the following conditions: undiagnosed abnormal genital bleeding; known, suspected, or history of breast cancer; known or suspected estrogen-dependent neoplasia; active deep vein thrombosis, pulmonary embolism, or history of these conditions; active or recent (within the past year) arterial thromboembolic disease (eg, stroke and myocardial infarction); known liver dysfunction or disease; or known or suspected pregnancy. There is no indication for Bithena in pregnancy.

The adverse reactions that occurred in at least 3% of Bithena-treated and placebo-treated postmenopausal women in a 12-week, randomized, double-blind, placebo-controlled trial, regardless of relationship to study drug, included vulvovaginal mycotic infection, upper respiratory tract infection, headache, and hot flush.

Bithena Vaginal Cream 1 gram is administered intravaginally daily for 1 week followed by 1 gram administered intravaginally twice weekly for the treatment of moderate-to-severe vaginal dryness and moderate-to-severe pain with intercourse, symptoms of vulvar and vaginal atrophy, due to menopause.

Please see accompanying full prescribing information, including Boxed Warning.

Bithena™ is generally well tolerated by postmenopausal women

Incidence of treatment-emergent adverse events occurring in >3% of patients (safety cohort)[1]

Adverse Events	1 g Placebo Cream (N=155)		1 g Bithena (N=150)	
	n	%	n	%
Infections and Infestations				
Vulvovaginal mycotic infection	5	3.2	7	4.7
Upper respiratory tract infection	7	4.5	7	4.7
Nervous System Disorders				
Headache	0	0.0	6	4.0
Vascular Disorders				
Hot flush	2	1.3	5	3.3

- Bithena was generally well tolerated by postmenopausal women in a clinical study, as demonstrated by a very low incidence of adverse events[1]
- Discontinuation for any reason was lower with Bithena (8.0%) vs placebo cream (11.6%)[2]

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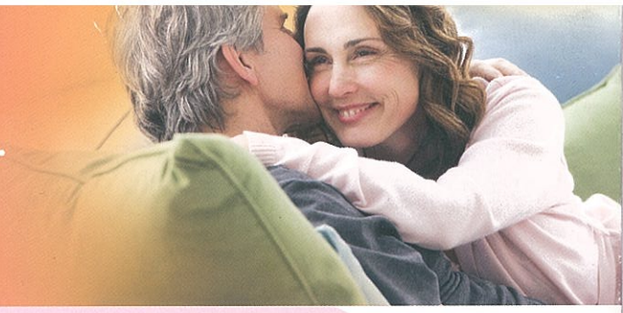

When moderate-to-severe symptoms of vulvar and vaginal atrophy due to menopause interrupt her life...

Bithena™ is designed with simple comfort in mind

SIMPLE DOSING

- 1 dose effective for all indications
- 0.625 mg synthetic conjugated estrogens, A per gram of Bithena
- Recommended dosage is 1 gram intravaginally daily for 1 week, followed by 1 gram intravaginally twice weekly[1]

SIMPLE APPLICATION

- Unique "click & lock" applicator ensures precise fill with every dose for less risk of overfill
- Only a prescription for Bithena provides patient with 8 applicators
- Low volume of cream (1 gram) minimizes messiness
- Cream formulation can be directly applied to vaginal and vulvar tissues for soothing relief

Bithena Vaginal Cream is indicated for the treatment of moderate-to-severe dyspareunia and vaginal dryness, symptoms of vulvar and vaginal atrophy, due to menopause.[1]

8 "click & lock" applicators

Not actual size.

References: 1. Bithena [prescribing information]. Duramed Pharmaceuticals, Inc; Pomona, NY: 2009.
2. Data on file, Duramed Pharmaceuticals, Inc.

Please see Important Safety Information on pages 2-3.

Please see accompanying full prescribing information, including Boxed Warning.

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Bring comfort back.

www.bithena.com

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